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Flaws in the LNT single-hit model for cancer risk: An historical assessment

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Abstract

The LNT single-hit model was derived from the Nobel Prize-winning research of Herman J. Muller who showed that x-rays could induce gene mutations in Drosophila and that the dose response for these so-called mutational events was linear. Lewis J. Stadler, another well-known and respected geneticist at the time, strongly disagreed with and challenged Muller's claims. Detailed evaluations by Stadler over a prolonged series of investigations revealed that Muller's experiments had induced gross heritable chromosomal damage instead of specific gene mutations as had been claimed by Muller at his Nobel Lecture. These X-ray-induced alterations became progressively more frequent and were of larger magnitude (more destructive) with increasing doses. Thus, Muller's claim of having induced discrete gene mutations represented a substantial speculative overreach and was, in fact, without proof. The post hoc arguments of Muller to support his gene mutation hypothesis were significantly challenged and weakened by a series of new findings in the areas of cytogenetics, reverse mutation, adaptive and repair processes, and modern molecular methods for estimating induced genetic damage. These findings represented critical and substantial limitations to Muller's hypothesis of X-ray-induced gene mutations. Furthermore, they challenged the scientific foundations used in support of the LNT single-hit model by severing the logical nexus between Muller's data on radiation-induced inheritable alterations and the LNT single-hit model. These findings exposed fundamental scientific flaws that undermined not only the seminal recommendation of the 1956 BEAR I Genetics Panel to adopt the LNT single-hit Model for risk assessment but also any rationale for its continued use in the present day.

Personal name as subject

- Herman J Muller
- Lewis J Stadler
- Barbara McClintock

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